Appln No.: 09/678,357
Amendment Dated: May 24, 2004
Reply to Office Action of May 19, 2003

REMARKS/ARGUMENTS

This is in response to the Office Action mailed May 19, 2003 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Corrected drawings are attached.

Claim 14 has been amended to include the limitations of claim 16, and other claims have been amended or canceled to conform to this amendment.

Claims 14-43 are pending in this application. Claims 14, 15, 24-30, 32, and 33-38 are rejected under 35 USC § 102(b) as anticipated by Lindgren. This rejection is rendered moot by the amendment to claim 14.

In viewing the present application, the Examiner is tending to take the view that more tests are better. This is not only counterintuitive from a cost perspective, but it fails to take into account the complexity associated with gastritis. Commonly Helicobacter pylori first colonize the antral part of the gastric mucosa where no acid secretion occurs. An occurrence of H.p.-Abs indicates an on-going or previous infection in the mucosa, either in the antral part, or antral plus corpus parts. There is no way to give a precise localization of the infection. Pepsinogen I and H,K-ATPase are localized in the corpus mucosa. At normal conditions PGI and H,K-ATPase-Abs show low levels in the blood. So, increased blood (serum) levels of PGI and/or H,K-ATPase-Abs are indicative of an inflammation in the corpus part of the mucosa. Together with the occurrence of H.p.-Abs, increased blood (serum) levels of PGI or H,K-ATPase-Abs are indicative of a pangastritis. The occurrence of H,K-ATPase-Abs are indicative of an autoimmune reaction. In some patients a transition occurs to an atrophy of the corpus mucosa. This means that there is a transition state from high levels of PGI, passing through the normal range and then to very low levels. Most of these patients have very high titres of H,K-ATPase-Abs. In addition, there are obviously conditions, e.g., absence of food in the stomach for a long period of time (Sundbom M, Mardh E, Mardh S, Ohrvall M, Gustavsson S. Reduction in serum pepsinogen I after Roux-en-Y gastric bypass. J Gastrointest Surg. 2003 May-Jun;7(4):529-35), where PGI levels are reduced. Therefore reduced PGI levels only may not be a sufficient indicator of atrophy.

The present invention makes use of a combination of tests for the three analytes to provide improved diagnosis of various types of gastritis in relation to each one of the individual analytes. A high degree of overlapping results in various types of gastritis when only individual analytes are employed is observed. A good resolution between the various groups of patients could, however, be demonstrated by the algorithm and using the combination of all three analytes plus the factor Hp x PGI in accordance with the present invention. This combination resulted

even in a good resolution between various types of gastritis when classified according to the Sydney system using gastroscopy plus histopathological examination of biopsies (Tables 1 and 2).

Claims 39-43 stand rejected as obvious over Lindgren. These kits contain the reagents for the performance of the multiple tests associated with the method of the invention. These tests are, as far as Lindgren is concerned duplicative at best, and indeed one test is shown to be better than the others. It would not be obvious by any sensible motivation to combine extra reagents for tests that Lindgren says are not needed to form a kit assembly. It would not increase convenience, only cost. Nor would it optimize diagnostic techniques, since following the full teaching of Lindgren one would merely through a portion of the reagents away.

Claims 14-43 are rejected as obvious over Oksanen and Ma. These reference teach separate assays for gastric, and the Examiner argues that combination of the assays would have been obvious. Contrary to the Examiner's apparent belief, "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." Carella v. Starlight Archery and Pro Line Co., 804 F.2d 135, 140, 231 USPQ 644, 647 (Fed. Cir. 1986) (citing ACS Hosp. Syss., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)). "[T]he factual inquiry whether to combine references must be thorough and searching." McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1351-52, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). This factual question cannot "be resolved on subjective belief and unknown authority," In re Lee, 277 F.3d 1338, 1343-44, 61 USPQ2d 1430, 1434 (Fed. Cir. 2002); "it must be based on objective evidence of record." Id. at 1343, 61 USPQ2d at 1434.

The burden is on the Examiner to establish a reason to do the assays from the separate references, and to show that there is an expectation from this art that the test results should be viewed in combination to arrive at a diagnosis and classification of the type of gastritis. Here the art as a whole (for example Lindgren et al) indicates a preference for single assays. Furthermore, the Examiner states that "limitations such as calculating ratios of indicators are viewed as limitations of optimizing experimental parameters." This is not substitute for a suggestion to calculate a product (not a ratio) of two results and use this as a diagnostic indicator. The Examiner must provide a reason, based on the references not some abstract principal, that this would be an obvious step in this particular case. Failing this, there is no prima facie case of obviousness. Thus, claim 14 and the claims dependent thereon are not obvious over this combination of references. Furthermore, the kit claims are also unobvious because there is no motivation to assemble all the reagents for the same reasons discussed above.

Claims 39-43 stand rejection as obvious over Lindgren in view of Harkonen. This rejection seems largely based on the erroneous interpretation of Lindgren as teaching a

methodology that uses all of the claimed reagents in an integrated test. This is not what Lindgren teaches. Lindgren's classification is based entirely on morphology. Table 1 reports serological test results for each morphology but makes no suggestion to do multiple tests to combine the results. Indeed, Lindgren concludes that one test is superior and leaves the artisan with no reason to do the others.

For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully Submitted,

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